Original Article

Survival Benefit of Single Fecal Immunochemical Test as Initial Screening for Colorectal Cancer in Two Districts in Roi Et Province, Thailand

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Objective: To determine a survival benefit from colorectal cancer [CRC] screening protocol that uses fecal immunochemical test (FIT) as initial screen, followed by colonoscopy for abnormal results.

Materials and Methods: Between November 2009 and March 2010, we enrolled 9,755 (out of 30,563) residents aged 50 years or older in the Phanomphrai and Nonghi, Roi Et, Thailand for fecal occult blood test [FOBTs] using FIT. Those with positive results were referred to the colonoscopy service at Roi Et Hospital. We analyzed the end point: CRC death up to 2016.

Results: Of 9,755 tested subjects, 828 (8.5%) had positive FOBT results, of whom 197 had abnormal pre-operative assessments. The remaining 631 were referred to the colonoscopy service, of whom 183 subsequently underwent polypectomy and 10 were found to have colorectal adenocarcinoma. No patients who had positive FIT results and underwent colonoscopy died of CRC, compared with 0.19% among those with negative FIT results, 2.03% among subjects who declined to undergo colonoscopy, and 0.14% for those who did not enroll in the initial screening program.

Conclusion: Single FIT followed by colonoscopy for positive results can detect early CRC and has a survival benefit as initial colorectal screening.

Keywords: Colorectal cancer screening, Fecal immunochemical test, Fecal occult blood test, Population-based screening

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Colorectal cancer [CRC] is the third most common cancer in men (746,000 cases, 10.0% of all cancers in men worldwide); and the second most common cancer in women (614,000 cases, 9.2% of all cancers in women worldwide)[1]. CRC is also one of the most common cancers in Thailand[2-4], and the second leading cause of death in the United States[5]. In 2015, Thailand had 4,104 deaths from CRC, 2,293 men and 1,811 women with an increasing trend[3]. Colonoscopic removal of adenomatous polyps prevents death from CRC[6], but currently Thailand has no nation-wide colonoscopy screening program. Fecal immunochemical test [FIT] has been studied as first-line screening tool[7], but is not yet covered by Thai national universal health coverage programs. Hence, our study investigated whether initial FIT testing at the community level, followed by colonoscopy for positive results, can yield survival benefits for CRC in rural Thailand.

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Materials and Methods

Settings

The study took place at Phanomphrai Hospital, a district hospital designated as a study

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base in collaboration with Chulabhorn Hospital. The hospital serves patients with in Phanomphrai and Nonghi, Roi Et, Northeastern Thailand.

Study participants

Between October 2009 and February 2010, we enrolled subjects aged 50 years or older with no history of CRC.

Fecal immunochemical test [FIT] as primary screening modality.

Village health volunteers and primary care staffs collected specimens at health centers in the community level, which were sent to a laboratory at Phanomphrai Hospital where FITs were tested. FITs were performed using one-step test device (SD BIOLINE FOB; sensitivity: 98%; specificity: 98.5%). The test has a detection limit at 50 ng/ml of human hemoglobin[8].

Diagnostic colonoscopy and pathological diagnosis

Colonoscopies for those with positive FIT results were provided at Roi Et Hospital, a 700-bed tertiary care hospital. Seven volunteer colonoscopists came from Chulalongkorn, Siriraj, Rajavithi, and Chulabhorn Hospitals, and four colonoscopists were from Roi Et Hospital. Specimens were sent to Chulabhorn Hospital in Bangkok for pathological studies.

Statistical analysis

Data are reported as means and standard deviations for continuous variables, and as percentages and absolute counts for categorical variables. All subjects were followed and checked for mortality status with monthly mortality reports from Phanomphrai and Nonghi District Registrars. Additional mortality status was checked with an application from NHSO UC Search Client version 1.4.7. (http://www.nhso.go.th/FrontEnd/index.aspx). Statistical analyses were performed using SPSS version 17.

This research had been approved by the Human Research Ethical Committee of Roi Et Provincial Office (certificate No. 2202/2012).

Results

Demographic characteristics

Within Phanomphrai and Nonghi, there were 30,563 residents aged 50 years or older, of whom we enrolled 9,755 (32.0%) participants, including 4,223 men and 5,532 women. Their mean age was 62.1±8.3 years (range: 50 to 97 years; Table 1).

Table 1. Demographic data (n = 9,755)

	Number	Percentage
Sex		
Male	4,223	43.3
Female	5,532	56.7
Age (years)	62.1±8.3 (50 to 97)	
50 to 59 years of age	4,223	43.3
60 to 69 years of age	3,628	37.2
70 to 79 years of age	1,596	16.4
≥80 years	306	3.1
BMI (kg/m^2)	22.7±3.8 (13 to 41.3)	
<18.5	1,121	11.5
18.5 to 22.9	3,933	40.3
23.0 to 24.9	2,128	21.8
25.0 to 29.9	2,331	23.9
≥30	242	2.5

FIT screening results

Of the 9755 subjects, 828 (8.5%) had positive FIT results. Slightly more men had positive results than did women (8.7% vs. 8.3%). We excluded 197 participants with positive results who forewent colonoscopies because of medical conditions, such as pulmonary tuberculosis and electrolyte imbalance (Figure 1).

Colonoscopy results

Colonoscopies were provided for 631 patients (86.2%), of whom 448 (71.0%) had negative results, and 183 (29.0%) were found to have polyps or abnormal findings. Pathologic reports included hyperplasia (n = 38, 20.8%), adenoma or sessile serrated polyp (n = 119, 65.0%), malignancy (n = 10, 5.5%), and other pathological diagnosis (n = 16, 8.7%). The ten patients who had malignant results included three men and seven women (average age: 62.7 years; range: 57 to 70 years), and their results were reviewed by the Chulabhorn Hospital Tumor Board.

Follow-up of participants and survival of colorectal cancer cases

Of the 9,755 subjects tested between October 2009 and February 2010, 1,346 (13.8%) had died as of 31 December 2016, including 21 deaths from CRC (0.22%). None of these 21 deaths were of subjects who had positive FIT results and subsequently underwent colonoscopies. The 21 deaths included 17 (0.19%) who had negative FIT results and four (2.03%) who had

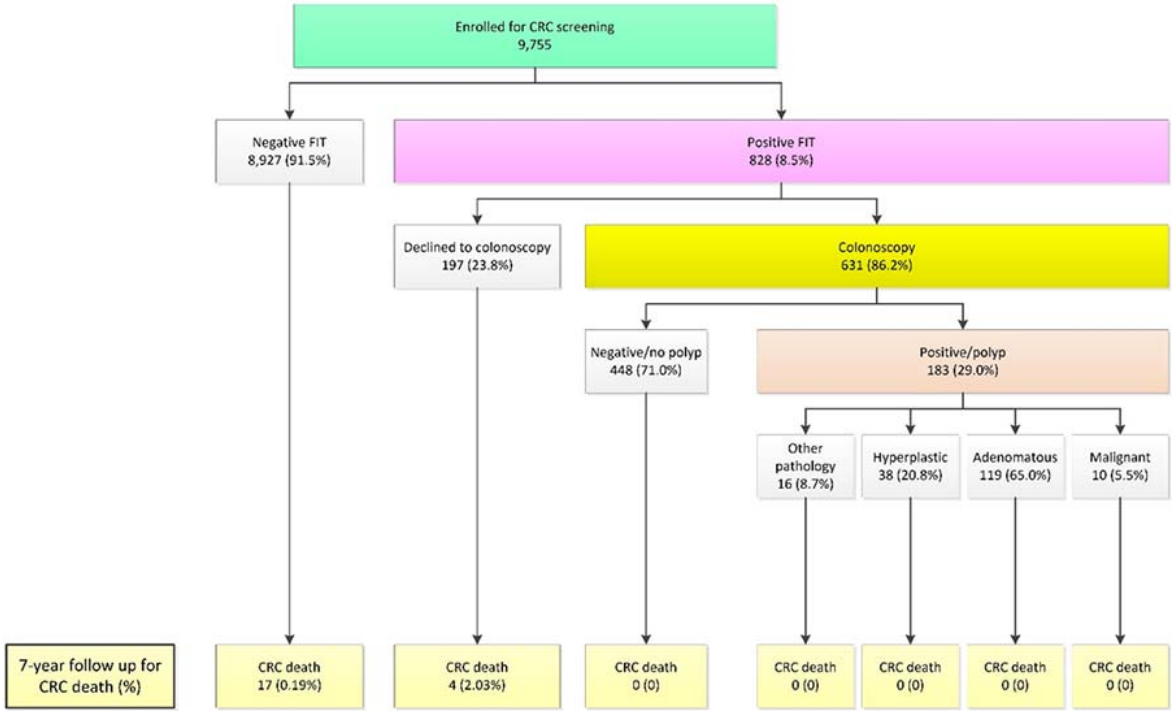

Figure 1 Flow of services and results of colorectal cancer screening project.

positive FIT results, but declined or was non-eligible to undergo colonoscopy. Among the non-enrolled group, 30 (0.14%) died from CRC.

Discussion

Colorectal cancer is an ideal target for population screening. It is a prevalent disease that can be detected and treated at an asymptomatic stage, leading to the reduced cancer mortality[9,10]. Compared with colonoscopy, FIT is not sensitive enough to detect CRC in asymptomatic individuals[11]. However, people are more likely to participate in screening with FIT than colonoscopy[12]. Annual FIT has been suggested as a screening method with better accuracy than the guaiac-based fecal occult blood test [gFOBT], and can be done with a single specimen[13].

During the time of our study, no national population-based scheme for CRC screening had been proposed. Compared with previous studies in Thailand, our study showed a higher rate of positive results (8.5% vs. 4.5% or 1.1%)[8,14]. This may be partly due to the different age group coverage, which included individuals aged 50 years or older (range: 50 to 97 years old), whereas the previous study cohorts comprised those aged only 50 to 65 years. Men participants showed higher positive results than did women (Table 3, 8.7% vs. 8.3%). Colorectal cancer and deaths from CRC could be prevented by colonoscopic removal of

Table 2. Area distribution

Area (sub-district)	Number	Percentage
Kutnamsai	301	3.1
Khoyai	299	3.1
Khamhai	492	5.0
Khoksawang	439	4.5
Chanuwan	363	3.7
Dukueng	936	9.6
Denrat	780	8.0
Nanuan	317	3.2
Phanomphrai	1,398	14.3
Phochai	401	4.1
Phoyai	494	5.1
Warisawat	575	5.9
Sakaeo	305	3.1
Saohae	308	3.2
Saensuk	834	8.5
Nongthapthai	706	7.2
Nonghi	807	8.3
Total	9,755	100.0

adenomatous polyps[15,16]. We saw no mortality after five years among individuals with positive FIT results who underwent colonoscopies.

Our study had some limitations, including low rate of screening colonoscopies among subjects with positive FIT results (76.2%)[17]. This was partly due to the non-eligible status found among subjects during pre-operative preparation, and to the high rate of coincidental diseases and disorders such as pulmonary tuberculosis and electrolyte imbalances. Other limitations consisted of no information for false-negative rate (as those with negative FIT results did not undergo colonoscopies). Furthermore, individual physicians' adenoma detection rates were not reported, so the quality of colonoscopic examination could not be measured[18]. In addition, improvement in CRC detection is not sufficient to improve screening outcomes[16,19]. Finally, colonoscopies were limited to CRC screening, including adherence to screening, periprocedural factors, intraprocedural factors, and risks of colonoscopy[16].

When compared with FIT, colonoscopy is considered cost-effective for screening adenoma, advanced neoplasia, and a composite endpoint of advanced neoplasia or stage I CRC[20]. The anatomical site distribution of our patients was three rectal, four sigmoid, one descending, and two transverse colon sites (Table 4). Six patients were classified as stage I disease, three as stage II, and one as stage III (Table 5). Nonetheless, shortage of colonoscopists is a major challenge for population-wide screening program.

Computed tomography colonography has evolved over the past two decades to become the primary alternative to optical colonoscopy for detection of colonic neoplasia, with good results in performance and reporting. The accuracy is compatible to optical colonoscopy for cancers and larger polyps[21,22]. The effect of screening with fecal occult-blood testing on CRC mortality persists after 30 years, but does not influence all-cause mortality[23].

Table 3. FIT screening results

Sex	FIT	
	Positive, n (%)	Negative, n (%)
Male	369 (8.7)	3,854 (91.3)
Female	459 (8.3)	5,073 (91.7)
Total	828 (8.5)	8,927 (91.5)

Table 4. Anatomical site distribution of findings

Site	Cancer
Rectum	3
Sigmoid colon	4
Descending colon	1
Transvers colon	2
Total	10

Table 5. Colonoscopy results

Histopathology	Number	Percentage
Colorectal cancer	10	1.6
Adenoma or sessile serrated polyp	119	18.9
Hyperplastic polyp	38	6.0
Other pathological diagnosis	16	2.5
No colorectal tumor	448	71.0
Total	631	100.0

Table 6. Staging and 5-year survival rates of 10 CRC cases

Stage	n	(%)
CRC-total	10	100
I	6	100
II	3	100
III	1	100
5-year survival rate	10	100

Table 7. 5-year follow-up in Phanomphrai and Nonghi Districts, Roi Et Province, Thailand

Group	Number	CRC death	CRC death rate (percentage)*
Enrollment group	9,755	21	0.22
FIT positive	828	4	0.48
Colonoscopy	631	0	0
Declined to colonoscopy	197	4	2.03
FIT negative	8,927	17	0.19
Non-enrollment group	20,808	30	0.14

* Note: the quality of data of cause of death at Phanomphrai and Nonghi Districts is in development with assistance from Bureau of Policy and Strategy, Ministry of Public Health, The Kingdom of Thailand. Currently the quality is around 35%

Our study suggested that we could optimize our limited colonoscopy resources by first-line testing with FIT screening, then colonoscopies only for those with positive FIT results. This approach may be a useful compromise in countries with shortages of colonoscopists. Hence, countries with medical resources similar to those in Thailand should consider this strategy to optimize population screening for CRC.

Conclusion

Single FIT followed by colonoscopy for positive results can detect CRC and has survival benefit. This screening strategy may be especially suitable in settings with limited colonoscopy service. Multiple annual FITs should be considered to increase screening yield.

What is already known on this topic?

Thailand has limited resources for starting population-based colorectal cancer screening.

What this study adds?

Population-based CRC screening can be possible with FIT as first-line testing and colonoscopy services provided only for those with positive results.

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Abbreviations

CRC = colorectal cancer; FIT = fecal immunochemical test; iFOBT = immunochemical fecal occult blood test.

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Availability of data and materials

Researchers wishing to access the data for this study should contact the corresponding author.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

Potential conflicts of interest

The authors declare no conflicts of interest.

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